Natriuretic peptide-induced relaxation of myometrium from the pregnant guinea pig is not mediated by guanylate cyclase activation.

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We tested both relaxation and cGMP generation by atrial (ANP), brain (BNP), and C-type natriuretic peptide (CNP) in oxytocin-stimulated myometrium from near-term pregnant guinea pigs to investigate the ability and mechanism of natriuretic peptides to inhibit myometrial contractility. Myometrial strips were contracted by 10(-8) M oxytocin, and relaxation to the cumulative addition (10(-9)-10(-6) M) of the natriuretic peptides measured. Maximal relaxation to BNP was significantly greater than to ANP (52 versus 32% respectively; $p < 0.05$), whereas CNP failed to produce relaxation. However, the increase in cGMP produced by BNP (10(-7) M) was significantly less than that produced by ANP (10(-7) M) (4.5 versus 7.0 times basal; $p < 0.05$); CNP did not increase myometrial cGMP. Anantin, a competitive blocker of the guanylate cyclase A receptor, significantly reduced the increase in cGMP produced by ANP and BNP, but had no effect on relaxation induced by either peptide. Rp-8-Br-cGMP, an inhibitor of the cGMP-dependent protein kinase, did not alter BNP-induced relaxation. The atrial natriuretic peptide-fragment 4-23 amide, a natriuretic peptide clearance receptor agonist, failed to inhibit oxytocin-stimulated myometrial contraction. We conclude that natriuretic peptide induced relaxation of oxytocin-stimulated myometrium from the pregnant guinea pig is not mediated by either guanylate cyclase A or B activation, is independent of the cGMP pathway, and does not involve clearance receptor activation. Our results suggest that natriuretic peptide-induced relaxation of pregnant myometrium is mediated via a novel mechanism.

PMID: 11259543 [PubMed - indexed for MEDLINE]

☐ 4: Postepy Hig Med Dosw 2000;54(6):895-914 Related Articles, Books

[N-terminal atrial natriuretic peptides].

[Article in Polish]

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Atrial myocytes synthesise atrial natriuretic factor prohormone consisting

of 126 amino acids (ANP1-126) which is subsequently processed to several fragments. Atrial natriuretic factor (ANF, ANP99-126) originating from the C-terminal portion of prohormone is a best described atrial peptide. However, several peptides originating from the N-terminus of this precursor also circulate and produce significant diuresis, natriuresis and vasodilatation. These are: long acting natriuretic peptide (ANP1-30), vessel dilator (ANP31-67) and kaliuretic peptide (ANP79-98). ANP1-98 and ANP68-98 also circulate. Kaliuretic peptide specifically stimulates urinary potassium excretion. These peptides are slowly metabolised and their plasma concentration is higher than ANF suggesting their important role in water-electrolyte homeostasis and regulation of vascular tone. N-terminal atrial peptides don't bind to classical natriuretic peptide receptors, each of them has probably its own unique receptors. Although these peptides activate particulate guanylate cyclase in a number of tissues, some of their effects, for example natriuresis, are not mediated by cGMP but rather by prostaglandin E2. Plasma concentration of N-terminal atrial peptides may be useful in diagnosis and risk stratification in patients with heart failure and after myocardial infarction. Recently N-terminal fragment of brain natriuretic peptide (BNP1-76) was identified in the blood. This peptide is secreted together with its C-terminal partner, BNP77-108 by ventricular myocytes. Some studies suggest that N-terminal BNP may be also a useful diagnostic tool in cardiovascular diseases.

Publication Types:
- Review
- Review, tutorial

PMID: 11227384 [PubMed - indexed for MEDLINE]

☐ 5: Life Sci 1999;65(10):1027-33 Related Articles, Books

Priming of superoxide anion in polymorphonuclear neutrophils by brain natriuretic peptide.

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In acute coronary syndromes such as unstable angina and myocardial infarction, serum concentration of brain natriuretic peptide, a cardiac hormone with potent vasodilatatory, natriuretic and diuretic activities, is elevated. Little is known about the effect of elevated BNP plasma concentration on free radical-mediated tissue damage in these states. We investigated the influence of human BNP 32 and its fragment BNP 7-32 on the production of superoxide anion by PMN, a major cause for myocardial damage. Although BNP showed itself no stimulatory